

RESEARCH MONOGRAPH . COMPOUND PROFILE

Procaine

The original synthetic local anesthetic introduced in 1905 as Novocaine, displaced by amide agents but retaining historical and reference status.

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COMPOUND CLASS	Ester local anesthetic (short-acting)

ABSTRACT

Procaine (2-(diethylamino)ethyl 4-aminobenzoate; CAS 59-46-1; molecular formula $C_{13}H_{20}N_2O_2$; molecular weight 236.31) is the original synthetic local anesthetic, synthesized by Alfred Einhorn at the University of Munich in 1905 and marketed by Hoechst as Novocain. The compound was developed as a cocaine substitute that lacked the abuse liability and addictive potential of the natural alkaloid; the ester linkage between the aromatic ring and the amino alcohol substantially reduces lipophilicity relative to cocaine while preserving sodium channel block. Procaine was the dominant local anesthetic from 1905 through approximately the 1950s, when lidocaine and the amide class displaced it owing to faster onset, longer duration, and substantially lower allergic reaction incidence. The principal limitation of procaine and the ester class is hydrolysis by plasma cholinesterase to para-aminobenzoic acid (PABA), the dominant allergen in the class and a substrate for hapten-mediated immune reactions in sensitized individuals. The plasma half-life is short (less than 1 minute through cholinesterase clearance); duration of clinical infiltration block is 30 to 60 minutes, much shorter than amide agents. Mechanism is voltage-gated sodium channel block with state-dependent kinetics; the lower lipid solubility relative to amide agents corresponds to slower onset and weaker block per milligram. Maximum recommended dose is 7 mg/kg, with adjustment for patients with cholinesterase deficiency (prolonged duration, increased systemic exposure). Modern clinical use is limited to short-procedure infiltration in patients with documented amide allergy and to several dental applications in markets where the ester formulations remain available. Procaine

penicillin (combined with penicillin G as a depot) extends antibiotic plasma levels and is the oldest application of procaine in formulation.

1. Compound Identification

Procaine is described as ester local anesthetic (short-acting). The original synthetic local anesthetic introduced in 1905 as Novocaine, displaced by amide agents but retaining historical and reference status.

1.1 Class summary

Ester local anesthetic (short-acting)

1.2 Subtitle

The original synthetic local anesthetic introduced in 1905 as Novocaine, displaced by amide agents but retaining historical and reference status.

2. Abstract

Procaine (2-(diethylamino)ethyl 4-aminobenzoate; CAS 59-46-1; molecular formula $C_{13}H_{20}N_2O_2$; molecular weight 236.31) is the original synthetic local anesthetic, synthesized by Alfred Einhorn at the University of Munich in 1905 and marketed by Hoechst as Novocain. The compound was developed as a cocaine substitute that lacked the abuse liability and addictive potential of the natural alkaloid; the ester linkage between the aromatic ring and the amino alcohol substantially reduces lipophilicity relative to cocaine while preserving sodium channel block. Procaine was the dominant local anesthetic from 1905 through approximately the 1950s, when lidocaine and the amide class displaced it owing to faster onset, longer duration, and substantially lower allergic reaction incidence. The principal limitation of procaine and the ester class is hydrolysis by plasma cholinesterase to para-aminobenzoic acid (PABA), the dominant allergen in the class and a substrate for hapten-mediated immune reactions in sensitized individuals. The plasma half-life is short (less than 1 minute through cholinesterase clearance); duration of clinical infiltration block is 30 to 60 minutes, much shorter than amide agents. Mechanism is voltage-gated sodium channel block with state-dependent kinetics; the lower lipid solubility relative to amide agents corresponds to slower onset and weaker block per milligram. Maximum recommended dose is 7 mg/kg, with adjustment for patients with cholinesterase deficiency (prolonged duration, increased systemic exposure). Modern clinical use is limited to short-procedure infiltration in patients with documented amide allergy and to several dental applications in markets where the ester formulations remain available. Procaine penicillin (combined with penicillin G as a depot) extends antibiotic plasma levels and is the oldest application of procaine in formulation.

3. Mechanism of Action

Voltage-gated sodium channel block, state-dependent, lower potency than amide class. Hydrolyzed by plasma cholinesterase to PABA (the dominant allergen).

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

7 mg/kg. Infiltration 1 to 2 percent.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Einhorn A. On the chemistry of local anesthetics. Munch Med Wochenschr 1905.
2. Covino BG. Pharmacology of local anaesthetic agents. Br J Anaesth 1986.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.